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The role of tumor cell chemosensitivity test in second-line or third-line chemotherapy in non-small cell lung cancer

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Background: In treatment of advanced non-small cell lung cancer, the effect of chemotherapy is limited and unpredictable. Especially in cases of recurrent or relapsed tumor, the choice of regimen is very restricted. This study was to determine whether the sensitivity test of chemotherapeutic agents is valuable in choosing the drugs of the second-line or third-line treatment in the advanced non-small cell lung cancer.

Methods: In 11 patients, resistant to or relapsed after the first-line or second-line chemotherapy, we got the tumor cells by the nine neck nodes or two bronchoscopic biopsies and did chemosensitivity test by the adenosine triphosphate-based chemotherapy response assay methods. The drugs tested were cisplatin, carboplatin, paclitaxel, docetaxel, gemcitabine, vinorelbine and irinotecan. We regarded the drug is sensitive in cases the cell death rate was above 30%, and chose two drugs of higher cell death rates as chemotherapeutic agents. After two cycles of chemotherapy, the response was evaluated.

Results: The mean age of the patients was 54.9 year, and one patient was excluded in the final analysis because the secondary tumor was proved as small cell lung cancer. Five patients were for the second-line and another five were for the third-line chemotherapy. Six tumors were sensitive to 3 drugs, 2 tumors were to two, and another two were to one agent. Cisplatin, gemcitabine, vinorelbine and irinotecan were sensitive in 5 cases respectively. Docetaxel was sensitive in 3 cases, paclitaxel and carboplatin were sensitive in 2 cases respectively. Regardless of the previous treatment, cisplatin kept the sensitivity in 4 of 8, gemcitabine in 2 of 3, and docetaxel in 1 of 3 cases. Complete response was found in 2 of 8 evaluable patients, and partial response was in 3, stable in 1, and disease progressed in 2 cases.

Conclusions: In cases of recurrent or resistant non-small cell lung cancer, chemosensitivity test would provide another options in choosing the chemotherapeutic agents.

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BCL-2, BCL-x_L, Survivin and P53 protein expression and response to the chemotherapy with cisplatin and etoposide in non-small cell lung cancerKarczmarek-Borowska, Bozenna¹ Filip, Agata² Gozdziuk, Kazimierz³ Drop, Andrzej⁴ Korobowicz, Elzbieta⁵ Wojciewski, Jacek² Sagan, Dariusz³

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Background: The identification of molecular markers useful for chemotherapy response assessment may help in treatment optimization of selected groups of patients that will benefit from the therapy and help to improve the therapy results. Markers that would be useful for predictive factors assessment in NSCLC are under investigation.

The aim of the study: Estimation of response to chemotherapy depending on BCL-2, BCL-x_L, Survivin and P53 protein expression.

Material and Methods: The group of 60 consecutive patients that were admitted to The Oncology Center of Lublin Land and to Department of Thoracic Surgery Medical University of Lublin was examined. The stage according to TNM was as follows: IIB - 26 cases (43,3%), IIIA - 34 cases (56,7%). Patients were treated with chemotherapy before planned surgery according to the schedule: cisplatin 30 mg/m² plus etoposid (PE) 100mg/m² for three consecutive days, every 21 days. The response to the therapy according to WHO was estimated. Protein expression was estimated by means of immunohistochemistry on paraffin tumor samples taken during surgery (the cut of was set on 10% of positive cells).

Results: Expression of BCL-2, BCL-x_L, Survivin and P53 proteins was found in 20%, 81,7%, 90% and 53,3% of cases, respectively. The percentage of positive cells (positive cytoplasmic or nuclear signal) in 500 tumor cells was estimated by semiquantitative method. Statistical analysis showed significant differences only in BCL-x_L and Survivin protein expression in response to chemotherapy. In patients that responded to the therapy we found less cells showing protein expression (p<0,05). There was no statistical significant correlation between median P53 protein expression and response to the chemotherapy, however low median per cent value of P53 positive cells was observed in patients that responded to the therapy.

Conclusion: High BCL-x_L and Survivin protein expression in tumor cells was found to be an important marker of lack of clinical response to the chemotherapy

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Impact of gender on median overall survival (MOS) in patients with advanced non-small cell lung cancer (NSCLC) treated with platinum-based chemotherapy- Single center experienceKhodadad, Kian¹ Zakeri, Azadeh² Masjedi, Mohammad R.³ Padyab, Mojgan⁴ Emami, Habib⁴

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Introduction: There is a debate on the impact of sex on survival of patients with advanced NSCLC. We retrospectively evaluated whether or not sex affects median overall survival (MOS) in patients with advanced NSCLC treated with 2nd or 3rd generation platinum-based regimens.

Patients and Methods: 230 patients with advanced NSCLC (unresectable IIIA/IIIB/IV) treated with 2nd or 3rd generation platinum-based chemotherapy was retrospectively analyzed for the impact of gender differences on MOS. Confounding factors (i.e. median age, stage and pathology) were also evaluated in both sexes.

Results: 181 men and 49 women were included in this analysis. There was no statistically significant difference in stage distribution (i.e. IIA/IIIB/IIIBw+IV) in both sexes (P=0.2). The difference in pathologic subtypes (undiff. NSCLC, Squam., Adenoca.) was statistically significant between women and men (15.1/9.4/75.5% and 25.6/31.8/42.6, respectively) (P=0.1/0.001/0.001). Mean age was 53.2 ± 11 in women and 59.7 ± 11.7 in men (P<0.001). Although the median survival time was longer in women but it was not statistically significant (13.7 m vs

10.3 m, $P=0.14$). Response rate was 32.7% and 38.7% in women and men, respectively ($P=0.4$).

Conclusions: Based on this study the MOS was not statistically significant between women and men with advanced NSCLC treated with platinum based chemotherapy. Differences in pathologic subtype and mean age may translate this finding. To elucidate the impact of sex on MOS in patients with advanced NSCLC we need further well balanced studies.

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Docetaxel-induced interstitial pneumonitis (DIIP) in non-small cell lung cancer patients

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Background: Docetaxel is a taxane anticancer drug with activity against a broad range of cancers. Pulmonary toxicity is a well-known complication observed with several anticancer drugs. But, interstitial pneumonitis as a toxicity of docetaxel is very rare.

Methods: A total of 53 patients with non-small cell lung cancer who received chemotherapy including docetaxel from January 2006 to December 2006 were analyzed retrospectively.

Results: 9 out of 53 patients (17.0%) showed newly developed ground glass opacity with/without consolidation or reticular density on follow up chest CT scans during docetaxel therapy. The lesions were not thought to be associated with disease progression or pulmonary infection. Majority of patients who showed newly developed abnormal CT findings consistent with interstitial pneumonitis had worsened or newly appeared dyspnea with deterioration of lung function of restrictive pattern. In association with the chemotherapy regimens, 7 out of 9 patients with DIIP received weekly docetaxel (30-40mg/m²), and remaining 2 received non-weekly docetaxel (60-75mg/m²). Among 7 patients who received weekly docetaxel, docetaxel only (30mg/m²) were 4, and docetaxel (40mg/m²) combined with cisplatin (35mg/m²) were 3. In association with the cumulative dose of docetaxel, below 60mg/m² was none, between 60 and 120 mg/m² was 1, between 120 and 240 mg/m² were 4, and between 240 and 480mg/m² were 4. The locations of abnormal radiographic findings were mainly peripheral (8 out of 9) and upper lobe (7 out of 9). For the treatment of DIIP 4 out of 9 patients received corticosteroid treatment, and all 4 patients showed symptomatic improvement.

Conclusions: DIIP developed in increasing frequency as the cumulative dose of docetaxel increased, especially with weekly regimen. Special concern should be given to the development of DIIP during docetaxel chemotherapy as its cumulative dose increases. DIIP should be included in differential diagnosis of newly developed radiographic abnormalities such as ground glass opacity or consolidation during docetaxel treatment especially if the lesion is peripheral and upper lobe predominant. For more clear clarification of DIIP, further prospective study of large scale is required.

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A phase II study of the combination chemotherapy of Docetaxel and Carboplatin in advanced non-small cell lung cancer

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Background: To evaluate the efficacy and safety of induction chemotherapy with docetaxel and carboplatin in advanced lung cancer.

Methods: Between January 2005 and January 2007, 54 patients were enrolled and evaluable. Patients were treated with Docetaxel 75mg/m² and Carboplatin AUC 5 on day 1 every 21 days.

Result: The median age was 62 (range 23-79) years old. Among the 54 patients, 51 were male. Pathologically, 19 patients had adenocarcinoma, 19 patients had squamous carcinoma and 3 patients had large cell carcinoma. Complete responses (CR) were in 2(3.7%) patients and partial responses (PR) in 26(48.14%) patients. The overall response rate was 51.85% and the median response duration was 5 (range, 1 to 12.7) months. The median progression-free survival was 10.5 (range, 1.4 to 19.5) months. The median overall survival for all patients was 14.8 (range, 1.4 to 23.8) months.

During a total 253 cycles, anemia greater than CTC grade 2 occurred in 51 cycles (20.15%), leukopenia occurred in 22 cycles (8.69%) and thrombocytopenia occurred in 19 cycles (7.5%). Non-hematologic toxicities were minor and easily controlled.

Conclusion: The combination chemotherapy of docetaxel and carboplatin has moderate efficacy with acceptable toxicities in patients with advanced NSCLC.

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The efficacy and characteristics of palliative chemotherapy for elderly patients with advanced or recurrent non-small cell lung cancer

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Background: We conducted retrospective analysis to evaluate the efficacy and characteristics of palliative chemotherapy for elderly patients with advanced or recurrent non-small cell lung cancer (NSCLC).

Methods: Between Mar 2000 and Feb 2004, newly diagnosed chemotherapy-naïve patients with advanced or recurrent NSCLC were included. All patients were histologically or pathologically proven to be NSCLC, with performance status 0 to 2. Comorbidity was evaluated according to the Charlson's comorbidity index. All patients received platinum-based combination chemotherapy (containing paclitaxel or gemcitabine) as the first-line treatment. The old age group was defined as patients with 65 years or more of age.

Results: Total 404 patients were retrospectively analyzed. The number of patients in the young age and the old age group were 283 (70%) and 121 (30%), respectively. The average number of total regimens (2.31 of old age vs. 2.81 of young age, respectively; $p<0.001$) and cycles (8.78 vs. 10.69, $p=0.006$) per head were significantly less in the old age group than in the young age group. Average administered doses of paclitaxel (119.3 vs. 137.4 mg/m², $p<0.001$) and gemcitabine (1962.1 vs. 2216.7 mg/m², $p<0.001$) per cycle were lower in the old age group than